endocrine (type 1 diabetes, autoimmune adrenalitis) and nonendocrine (systemic lupus erythematosus, myasthenia gravis, and Sjögren syndrome; Chapter 6). They are also at increased risk for the development of extranodal marginal zone B-cell lymphomas within the thyroid gland (Chapter 13). The relationship between Hashimoto disease and thyroid epithelial cancers remains controversial, with some morphologic and molecular studies suggesting a predisposition to papillary carcinomas.

Subacute Lymphocytic (Painless) Thyroiditis

Subacute lymphocytic thyroiditis, which is also referred to as *painless thyroiditis*, usually comes to clinical attention because of mild hyperthyroidism, goitrous enlargement of the gland, or both. Although it can occur at any age, it is most often seen in middle-aged adults and is more common in women. A disease process resembling painless thyroiditis can occur during the postpartum period in up to 5% of women *(postpartum thyroiditis)*. Painless and postpartum thyroiditides are variants of autoimmune thyroiditis. Most of the patients have circulating antithyroid peroxidase antibodies or a family history of other autoimmune disorders. As many as a third of cases can evolve into overt hypothyroidism over time, and the thyroid histology may resemble Hashimoto thyroiditis.

MORPHOLOGY

Except for possible mild symmetric enlargement, the thyroid appears grossly normal. Microscopic examination reveals lymphocytic infiltration with large germinal centers within the thyroid parenchyma and patchy disruption and collapse of thyroid follicles. Unlike Hashimoto thyroiditis, however, fibrosis and Hürthle cell metaplasia are not prominent.

Clinical Course. Affected individuals may present with a painless goiter, transient overt hyperthyroidism, or both. Some patients transition from hyperthyroidism to hypothyroidism before recovery. As stated, as many as a third of affected individuals eventually progress to overt hypothyroidism over a 10-year period.

Granulomatous Thyroiditis

Granulomatous thyroiditis (also called *De Quervain thyroiditis*) occurs much less frequently than does Hashimoto disease. The disorder is most common between the ages of 40 and 50 and, like other forms of thyroiditis, affects women considerably more often than men (4:1).

Pathogenesis. Granulomatous thyroiditis is believed to be triggered by a viral infection. The majority of patients have a history of an upper respiratory infection just before the onset of thyroiditis. The disease has a seasonal incidence, with occurrences peaking in the summer, and clusters of cases have been reported in association with coxsackievirus, mumps, measles, adenovirus, and other viral infections. Although the pathogenesis of the disease is unclear, one model suggests that it results from a viral infection that leads to exposure to a viral or thyroid antigen secondary to virus-induced host tissue damage. This antigen stimulates cytotoxic T lymphocytes, which then damage thyroid follicular cells. In contrast to autoimmune thyroid disease, the immune response is virus-initiated and not self-perpetuating, so the process is limited.

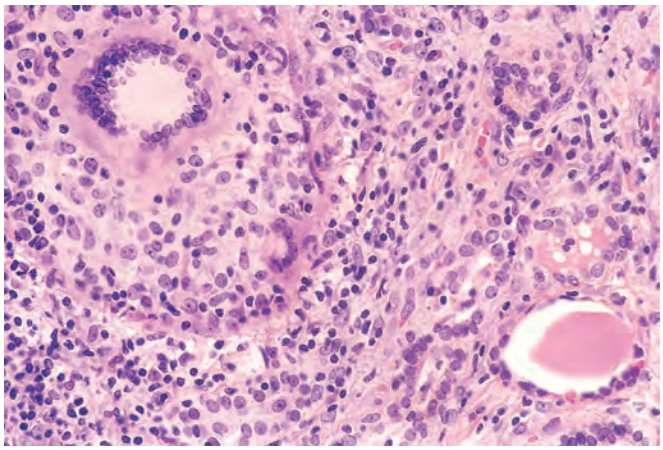

Figure 24-12 Granulomatous thyroiditis. The thyroid parenchyma contains a chronic inflammatory infiltrate with a multinucleate giant cell *(above left)* and a colloid follicle *(bottom right)*.

MORPHOLOGY

The gland may be unilaterally or bilaterally enlarged and firm, with an intact capsule that may adhere to surrounding structures. On cut section, the involved areas are firm and yellow-white and stand out from the more rubbery, normal brown thyroid substance. Histologic changes are patchy and depend on the stage of the disease. Early in the active inflammatory phase, scattered follicles may be disrupted and replaced by neutrophils forming microabscesses. Later, more characteristic features appear in the form of aggregates of lymphocytes, activated macrophages, and plasma cells associated with collapsed and damaged thyroid follicles. **Multinucleate giant cells** enclose naked pools or fragments of colloid (Fig. 24-12), hence the designation **granulomatous thyroiditis**. In later stages of the disease a chronic inflammatory infiltrate and fibrosis may replace the foci of injury. Different histologic stages are sometimes found in the same gland, suggesting waves of destruction over a period of time.

Clinical Course. Granulomatous thyroiditis is the most common cause of *thyroid pain*. There is a variable enlargement of the thyroid. Inflammation of the thyroid and hyperthyroidism are transient, usually diminishing in 2 to 6 weeks, even if the patient is not treated. Nearly all patients have high serum T_4 and T_3 levels and low serum TSH levels during this phase. However, unlike in hyperthyroid states such as Graves disease, radioactive iodine uptake is diminished. After recovery, generally in 6 to 8 weeks, normal thyroid function returns.

Other, less common forms of thyroiditis include *Riedel thyroiditis*, a rare disorder characterized by extensive fibrosis involving the thyroid and contiguous neck structures. The presence of a hard and fixed thyroid mass clinically simulates a thyroid carcinoma. It may be associated with fibrosis in other sites in the body, such as the retroperitoneum, and appears to be another manifestation of a